UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,807	02/02/2006	Bernard Fromenty	125649	7793

25944 7590 12/04/2008

OLIFF & BERRIDGE, PLC
P.O. BOX 320850
ALEXANDRIA, VA 22320-4850

EXAMINER	
POLANSKY, GREGG	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
12/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,807	FROMENTY ET AL.	
	Examiner	Art Unit	
	GREGG POLANSKY	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *2,4-7,10-13,21-27 and 29-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,8,9,14-20,28 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/18/2005, 1/04/2006 & 2/02/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicants' preliminary amendments, filed 10/18/2005, amending Claims 5, 12-28, 33, 34, and 36, are acknowledged.

2. Applicants' Information Disclosure Statements, filed 10/18/2005, 1/04/2006 and 2/02/2006, are acknowledged and have been reviewed.

3. Applicants' election with traverse of Group I (Claims 1, 3, 5-20, 22-28, and 37) and the specie "obesity", in the reply filed on 9/18/2008, is acknowledged. The traversal is on the ground that in Applicants' view, the Office has not demonstrated an *a priori* unity of invention as stated in the Restriction Requirement. Applicants argue that β-aminoisobutyric acid is not the common subject matter between the claims.

4. Applicants' argument that β-aminoisobutyric acid is not the common subject matter between the claims has been considered but are not persuasive. As presented in the Requirement for Restriction, the Office considers β-aminoisobutyric acid to be the common technical feature among the claims and has provided art demonstrating knowledge of β-aminoisobutyric acid prior to the instant invention. With regard to Applicants arguments to the election of species requirement, the instant Specification fails to disclose what diseases "are linked to the accumulation of triglycerides in tissues and blood" as required by the instant claims. Therefore one could not reasonably determine which diseases are so linked and read on the instant claims. The Restriction Requirement is still deemed to be proper and is therefore made Final.

5. Claims 2, 4, 21, and 29-36 are withdrawn from consideration in accordance with 37 CFR 1.142(b), because they are contained in non-elected groups.

6. Claims 5-7, 10-13, and 22-27 are withdrawn from consideration in accordance with 37 CFR 1.142(b), because they are drawn to non-elected species. The requirement is still deemed proper and is thus made Final.

7. Claims 1-37 are pending.

8. Claim 1, 3, 8, 9, 14-20, 28 and 37 are presently under consideration.

9. It is noted that it does not appear the signatures on the Oath are by each Applicant's own hand. No action is required by Applicants.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1, 3, 8, 9, 14-20, 28 and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

The claims recite "β-aminoisobutyric acid, **derivative, prodrug, metabolite or complex thereof**" (emphasis added). There is insufficient written basis for β-aminoisobutyric acid derivatives, prodrugs, metabolites or complex thereof in the Specification.

Regarding the requirement for adequate written description of chemical entities, Applicant's attention is directed to MPEP §2163. In particular, *Regents of the University of California v. Eli Lilly & Co.,* 119 F.3d 1559, 1568 (Fed. Cir. 1997), *cert denied*, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plan for obtaining the claimed chemical invention." *Elli Liily*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications under the 35 U.S.C. 112.1 "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics when coupled with a known or disclosed correlation between function and structure…" *Enzo Biochem, Inc. v. Gen-Probe Inc.,* 296 F.3d 316, 1324-25 (Fed. Cir. 2002) (quoting *Guidelines*, 66 Fed. Reg. At 1106 (emphasis added)). Moreover, although *Elli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. *Univ. of Rochester v. G.D. Searle & Co.*, 249 Supp. 2d 216, 225 (W.D.N.Y. 2003).

The instant Specification discloses that "[t]he term 'derivatives' include[s] inorganic salts, esters or amides of β-aminoisobutyric acid". See page 6, last paragraph. The Specification further discloses that the "terminal carboxylic group of β-aminoisobutyric acid may be in particular under the form of an ester, for example lower alkyl ester, (in particular C_1-C_{10}) or of an amide". See page 7, 1st paragraph. These are merely exemplifications of derivatives of β-aminoisobutyric acid; there is no disclosure of a precise definition of what Applicants envisage as β-aminoisobutyric acid derivatives useful in the instant invention. Likewise, Applicants' definitions of metabolites and prodrugs of β-aminoisobutyric acid are lacking an adequate written description. Applicants disclose the term "metabolite" is defined to be "any substance resulting from the metabolism of BAIBA (β-aminoisobutyric acid) and the term "prodrug" is defined to be "any substance that gives rise to a pharmacologically active for of BAIBA although not itself active and excludes any peptide comprising BAIBA as amino-acid residue or pseudopeptide resulting from the coupling of BAIBA with non-peptidic entity, such as histamine". See page 7. The Specification does not provide a definition of the term "complex".

Applicants have failed to provide any structural characteristics, chemical formula, name(s) or physical properties of derivatives, prodrugs or metabolites of β-aminoisobutyric acid, aside from the exemplifications discussed above. As such, it is not apparent that Applicants were actually in possession of, and intended to use within the context of the present invention, any specific derivatives, prodrugs or metabolites of β-aminoisobutyric acid at the time the present invention was made. The skilled artisan

could not "immediately envisage" the claimed compounds based on the description in the disclosure.

12. Regarding Claims 1 and 20, Applicants have failed to disclose how a disease must be "linked" to an accumulation of triglycerides in tissues and blood to be treatable by the instant methods. Absent this disclosure, the skilled artisan could not "immediately envisage" the diseases or conditions treatable by the instant methods. Further, Applicants have failed to disclose a listing of the specific disease which they envisage as being treatable by the instant methods.

13. Claims 1, 8, 14-19, 20 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the Specification, while being enabling for treating obesity, does not reasonably provide enablement for the prevention of obesity or "diseases linked to the accumulation of triglycerides in tissues and blood". The Specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. This is a Scope of Enablement rejection.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in

the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The instant claims are drawn to a method of treating and/or preventing obesity and treating and/or preventing diseases "linked" to the accumulation of triglycerides in tissues and blood, of which obesity is one example, by administering an effective amount of β-aminoisobutyric acid or derivatives, prodrugs or metabolites thereof. The claims are very broad since they encompass the prevention of obesity of any etiology (Claim 8) and the prevention of all diseases "linked" to the accumulation of triglycerides (Claim 1).

(3) The state of the prior art:

The Merck Manual teaches that people are considered to be overweight when their body mass index (BMI) is over 25; a person with BMI of 30 or more is considered to be obese. See page 1, 1st 5 lines. The Merck Manual teaches that obesity "results from consuming more calories than the body uses". There are many factors that influence weight gain, including: genetic and environmental factors, physical inactivity, alcohol consumption, socioeconomics, menopause in women, stress, polycystic ovary syndrome, pharmaceuticals, and smoking cessation. See page 2.

(4) The predictability or unpredictability of the art and (5) the relative skill of those in the art:

The relative skill of those in the art of pharmacology and medicine and the unpredictability of the pharmacological and biological arts are very high. In fact, the courts have made a distinction between mechanical elements, which function the same in different circumstances, yielding predictable results, and chemical and biological compounds, which often react unpredictably under different circumstances. *Nationwide Chem. Corp. v. Wright*, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); *In re Fischer*, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art. Likewise, the physiological or pharmaceutical activity of preventing obesity (and other conditions "linked" to the accumulation of triglycerides"), particularly with regard to the multitude of factors which influence the development of obesity, is an unpredictable art.

Thus, it is not understood how one skilled in the art can reasonably expect that the instant compound can be administered in order to have the "preventive" effect.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The Specification has provided guidance and a working examples for the use of β-aminoisobutyric acid (but not for any derivatives, prodrugs, or metabolites thereof) for reducing weight gain and reduction of triglycerides in mice.

(8) The quantity of experimentation necessary:

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. *In re Fisher*, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. *In re Fisher*, 427 F.2d 839, 166 USPQ 24; *Ex Parte Hitzeman*, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a specification requires more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. *In re Wright*, 999 F.2d 1562-63, 27 USPQ2d 1575.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

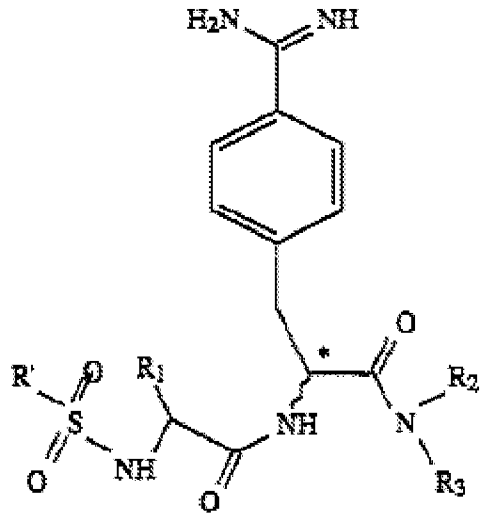
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1, 3, 8, 9, 14-20, and 28 rejected under 35 U.S.C. 103(a) as being unpatentable over Stüber et al. (U.S. Patent No. 5,457,114), in view of The Merck Manual (The Merck Manual, 17th Edition, 1999, "Thrombotic Disorders" and "Arteriosclerosis").

Stüber et al. teach compounds of formula I (below):



Wherein R_1 is a group of the structure A—B—C. C is derived from an N-bonded alpha, beta, gamma or delta amino acid and *inter alia* β-aminoisobutyric acid is taught as a suitable amino acid. See Abstract, and column 3, lines 1-5 and 41. The compound is taught as being useful as a pharmaceutical anticoagulant (thrombin inhibitor). See

column 2, lines 19-24. The compound can be in the form of a salt. See column 5, last paragraph. The compound would be considered to be a β-aminoisobutyric acid derivative.

The Merck Manual teaches "[p]atients with symptomatic atherosclerosis are at significant risk of stroke, MI, and peripheral artery occlusion" and that rupture of atherosclerotic plaques initiates thrombus formation. See page 920, "Atherosclerosis". The reference teaches anticoagulants useful in the treatment of thrombotic occlusions (clots). See page 918, 2nd column. The Merck Manual teaches that elevated LDL and reduced HDL lipids appear to be a causative factor of arteriosclerosis and that elevate triglycerides (hypertriglyceridemia) is a cause of reduced HDL. See page 1656, "Abnormal serum lipid levels". Further, the reference teaches obesity to be an independent risk factor for coronary artery disease (i.e. arteriosclerosis) and that hypertriglyceridemia "is commonly associated with obesity, diabetes mellitus, and insulin resistance". See last paragraph bridging pages 1656-1657.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the anticoagulant agents (which include derivatives of β-aminoisobutyric acid) taught by Stüber et al. to treat thrombotic disorders. Whereas The Merck Manual teaches arteriosclerosis increases the risk of thrombotic related conditions and hypertriglyceridemia (resulting in reduced HDL) is a causative factor of arteriosclerosis, treatment with the agents taught by Stüber et al. would naturally treat the instantly claimed diseases/conditions (i.e., obesity and disease "linked to the accumulation of triglycerides in tissues and blood"). It is noted that *In re Best* (195

USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention"). Also see *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1343-44, 74 USPQ2d 1398, 1406-07 (Fed. Cir. 2005) (holding that a prior art patent to an anhydrous form of a compound "inherently" anticipated the claimed hemihydrate form of the compound because practicing the process in the prior art to manufacture the anhydrous compound "inherently results in at least trace amounts of" the claimed hemihydrate even if the prior art did not discuss or recognize the hemihydrate).

Although the references are directed to treatment of human subjects, it would have been obvious to one of ordinary skill to treat any animal (i.e., agricultural, domestic

or laboratory animals, as required by instant Claims 17-19) subject to thrombotic related disorders with the compounds taught by Stüber et al.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

17. Claims 1, 3, 8, 9, 14-20, 28 and 37 are rejected.

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GREGG POLANSKY whose telephone number is (571)272-9070. The examiner can normally be reached on Mon-Thur 9:30 A.M. - 7:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregg Polansky/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614